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CANDIDATE RECOMBINATIONAL REPAIR GENES *XRCC3* AND *HH5RAD51* ARE YEAST *RAD51* HOMOLOGS,

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Mutant irs1SF, isolated from CHO AA8 cells based on its retarded growth after x-irradiation , has elevated spontaneous chromosomal aberrations and retarded rejoining of single-strand breaks[1]. In addition to a ~2.5 × difference in radiation sensitivity between mutant and wild-type cells at D_{10} (dose reducing survival to 10%), irs1SF is moderately sensitive to the alkylating agent EMS and to UV irradiation (2.5 × each) but extremely sensitive to cross-linking agents mitomycin C (MMC) (90 ×), nitrogen mustard, cisplatin, and melphalan (20-30 × each). Somatic cell hybrids of irs1SF and human lymphocytes showed correction by a gene localized to chromosome 14q32.3 and designated *XRCC3.* We isolated the *XRCC3* cDNA by co-transferring hygromycin B and MMC resistance to irs1SF[2]. Irs1SF cDNA transformants showed < 45% restoration of resistance to MMC, cisplatin, and γ radiation. In contrast, spontaneous chromosomal aberrations were corrected to > 90% wild-type level, and the plating efficiency was substantially enhanced. A cosmid clone containing the *XRCC3* gene was obtained from a chromosome 14 cosmid library kindly supplied by Larry Deaven (LANL). The gene structure shows 9 exons and 8 introns, with exonic sequence spanning 14,130 bp. Conceptual translation of the ORF reveals a 346 a.a. protein with ~ 25% identity to *S. cerevisiae* Rad51 and Rad57 proteins, which act in the Rad52 recombinational repair pathway. The similarities between XRCC3 and the yeast repair proteins argue that it also acts by recombinational repair to remove DNA cross-links and other lesions

We recently identified another member of the Rad51 protein family by searching EST databases. The new homolog, *HH5RAD51*, which also resides on chromosome 14, encodes a 350 a.a. protein that is related to XRCC3, with ~ 25% identify. XRCC3, in addition, shares homology with another distant Rad51 homolog XRCC2, which corrects the V79 mutant irs1.

In initial protein overexpression studies using *E. coli,* XRCC3 is insoluble.

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